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Preparation of Tetrahydropyran Derivatives with α-Electron-Withdrawing Substituents from 1,5-Dibromopentane Derivatives by Treatment with Silver Nitrate

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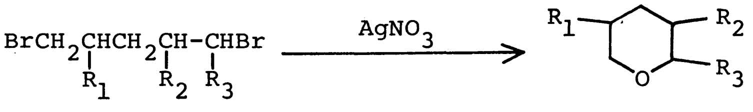
When 1,5-dibromopentane derivatives having the electron-withdrawing groups at one terminus, which were obtained by Cu(I)-catalyzed photochemical addition of 1,3-dibromopropanes to electron-deficient olefins, were subjected to treatment with silver nitrate, tetrahydropyran derivatives with the electron-withdrawing groups at the α-position to the oxygen atom were obtained.

Although a variety of methods have been proposed for direct preparation of substituted tetrahydropyrans from acyclic precursors, many of those necessitate rather hard reaction conditions such as presence of an acid or a free-radical initiator and are not often compatible with reactive functional groups. Methods from dihaloalkane derivatives have been known of only a few examples containing praparation of unsubstituted tetrahydropyran by treatment of 1,5-dibromopentane with zinc oxide in water for very long hours[1-3] and hard to afford tetrahydropyran derivatives with the α-electron-withdrawing substituents. We wish to report here our results that various substituted tetrahydropyrans with the electron-withdrawing groups at the α-position to the oxygen atom are derived by treatment with silver nitrate from 1,5-dibromopentane derivatives having the electron-withdrawing groups at one terminus, which are readily prepared by Cu(I)-catalyzed photochemical addition of 1,3-dibromopropane or its derivatives to electron-deficient olefins.[4] A variety of functional groups (e.g., CO_2R, vinyl, CN, and CHO) can be tolerated in our method.

2,6-Dibromohexanenitrile (1a), which was prepared from 1,3-dibromopropane and acrylonitrile, was first subjected to reaction with silver nitrate in CH_3CN-H_2O under reflux. 2-Bromo-6-nitroxyhexanenitrile, however, was only produced. In turn, 1a was treated with silver nitrate in DMSO-H_2O. After 1a (2 mmol) in DMSO (12 ml) was added to silver nitrate (6 mmol) in H_2O (15 ml), the resulting solution was heated at 110 °C for 3 h. After filtration of a precipitate, the reaction mixture was poured into water and extracted with ether. VPC analysis of the extract showed the presence of the only volatile product, which was isolated by silica-gel chromatography and assigned as 2-cyanotetrahydropyran (2a) by ^1H-NMR, IR, and mass spectra. The reaction of 1a with silver nitrate was performed in some other solvent systems (DMF-H_2O, dioxane-H_2O, and micellized benzene-H_2O) and the DMSO-H_2O system was proved to be the best of solvent systems examined (Table 1). Although 1a was treated with silver oxide instead of silver nitrate in DMSO-H_2O

and CH_3CN-H_2O, 2a was not produced at all. Preparation of various tetrahydropyrans is collected in Table 1.

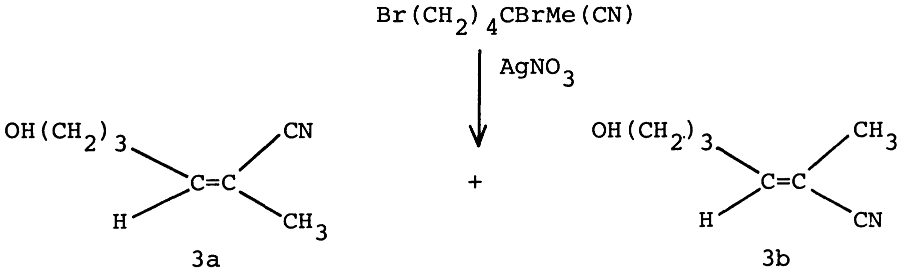
Table 1. Preparation of tetrahydropyrans from 1,5-dibromopentanes



1 2

	R_1	R_2	R_3	Solvent	Yield of 2 / %
a	H	H	CN	DMSO-H_2O	57
				CH_3CN-H_2O	0
				DMF-H_2O	0
				dioxane-H_2O	51
				benzene-H_2O-NaLS	0
b	H	H	COOEt	DMSO-H_2O	78
c	H	H	COMe	DMSO-H_2O	79
d	H	H	CHO	DMSO-H_2O	61
e	H	Me	CN	DMSO-H_2O	56
f	H	Me	COOEt	DMSO-H_2O	77
g	H	COOEt	COOEt	DMSO-H_2O	75
h	H	-$(CH_2)_3$CO-		DMSO-H_2O	72
i	Me	H	CN	DMSO-H_2O	57
j	$CH_2CH=CH_2$	H	CN	DMSO-H_2O	48
k	$CH_2CH=CH_2$	COOEt	COOEt	DMSO-H_2O	49

When 2-methyl-2,6-dibromohexanenitrile, in which one of the carbon atom bearing bromine is tertiary, was subjected to treatment with silver nitrate in DMSO-H_2O, cyclization did not occur and acyclic ene-ol compounds (3a, b) were produced [(3a), 67%;(3b), 10%].



3a 3b

This method was also tried for construction of the oxepane ring. Treatment of 2,7-dibromoheptanenitrile with silver nitrate in DMSO-H_2O gave 2-cyanooxepane in 10% yield.

References

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